The opinion in support of the decision being entered today is *not* binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte
EDMUND K. WALLER, CHRISTOPHER D. HILLYER, and JOHN ROBACK

Appeal 2007-0320
Application 09/945,339
Technology Center 1600

DECIDED: September 13, 2007

Before TONI R. SCHEINER, DONALD E. ADAMS, and LORA M. GREEN, *Administrative Patent Judges*.

SCHEINER, *Administrative Patent Judge*.

REMAND TO THE EXAMINER

Appellants appeal under 35 U.S.C. § 134 from the final rejection of claims 1-6 and 15-20.[1] We have jurisdiction under 35 U.S.C. § 6(b). On consideration of the record, we find that this case is not in condition for a decision on appeal. Accordingly, we remand the application to the Examiner to consider the following issues and to take appropriate action.

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[1] Claims 7-14 and 21-58 are also pending, but have been withdrawn from consideration.

BACKGROUND

"The present invention relates to a method of transplanting hematopoietic cells between genetically unrelated individuals using mononuclear cells treated so as to substantially reduce their ability to cause graft versus host disease while they retain their ability to proliferate in the recipient and facilitate engraftment by hematopoietic cells" (Spec. 1).

According to the Specification, "the treated mononuclear cells can condition the recipient to successfully accept the transplanted cells [ ] without mounting an immune response against the recipient's cells" and "[t]he mononuclear cells can also exert a graft versus leukemia effect by which they aid in the elimination of residual cancer cells in the recipient" (Spec. 22: 25 to 23: 2). In a nutshell, the Specification teaches that the ability of the treated mononuclear cells to proliferate in the recipient is directly proportional to the cells' ability to facilitate engraftment of transplanted hemaotpoietic cells, but inversely proportional to the cells' capacity to trigger GvHD (Spec. *passim*).

Claim 1 is representative of the subject matter on appeal:

1. A method of transplanting hematopoietic cells from a donor source into a genetically unrelated recipient, comprising:

a) administering to the recipient, in combination with the administration of the hematopoietic cells, an amount of mononuclear cells which are treated so as to substantially reduce their ability to cause graft versus host disease while they retain their ability to proliferate in the recipient and facilitate engraftment of the hematopoietic cells in the recipient; and

(b) administering to the recipient an effective amount of hematopoietic cells.

According to the present Specification,

- "[t]he mononuclear cells are incubated with a *sufficient concentration* of [a] cytotoxic drug so as to *substantially reduce their ability to cause graft versus host disease* while they retain their ability to *proliferate* in the recipient to enhance the recipient's ability to fight cancer, leukemia and viral infection" (Spec. 19: 11-15, emphasis added);

- "[a] '*sufficient concentration*' [of the cytotoxic drug] is that which causes greater than 90% inhibition of the proliferation of treated cells as measured by assays known in the art" (Spec. 19: 15-17);

- "the phrase 'substantially reduce their ability to cause graft versus host disease' means that as a result of treatment according to the methods of the invention, a given concentration of treated mononuclear cells administered to a recipient results in the absence of graft versus host disease, whereas the same concentration of untreated mononuclear cells administered to a recipient results in severe graft versus host disease" (Spec. 15: 24 to 16: 2); and

- "[b]y 'proliferation' is meant cell division that leads to an increase in the number of nucleated cells such that the number of cells and their progeny at, for example, time T + 1 is greater than the number of cells at time T" (Spec. 16: 11-13).

- Finally, "[b]y 'in combination' is meant the treated mononuclear cells can be administered to the recipient before, contemporaneously with, or after the administration of the hematopoietic cells to the recipient" (Spec. 15: 21-24).

Thus, based on the explicit teachings of the Specification, claim 1 requires that the treated mononuclear cells retain their ability to proliferate,

but their ability to proliferate must be reduced by more than 90% in order to substantially reduce their ability to cause graft versus host disease.

The Rejection

The Examiner rejected claims 1-6 and 15-20 under 35 U.S.C. § 103(a) as unpatentable over Waller[2] in view of Sykes.[3]

Waller describes "a method of transplanting hematopoietic system reconstituting cells from a donor to an antigenically matched or unmatched, genetically unrelated recipient or an antigenically unmatched, genetically related recipient with successful engraftment in the *absence* of GvHD" (Waller, col. 2, l. 66 to col. 3, l. 3 (emphasis added)). Waller's method comprises "administering to the recipient, prior to the administration of the hematopoietic . . . cells, an amount of mononuclear cells which are treated so as to render them incapable of proliferating and causing a lethal GvHD effect, but which are effective in enhancing subsequent engraftment of the hematopoietic . . . cells in the recipient" (*id.* at col. 3, ll. 8-14). The mononuclear cells can be treated, "for example by exposure to a source of ionizing radiation" (*id.* at col. 4, ll. 43-44), or "with cytotoxic chemotherapeutic drugs" (*id.* at 4, ll. 66-67) including fludarabine (*id.* at 5, l. 11).

On first impression, Waller's disclosure seems plain enough: "The mononuclear cells are 'treated so as to render them *incapable of proliferating* and causing a lethal GvHD effect'" (Waller, col. 4, ll. 40-41

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[2] U.S. Patent 5,800,539 to Waller, issued September 1, 1998.
[3] WO 99/25367, International Patent Application of Sykes, published May 27, 1999.

(emphasis added)). However, Waller immediately qualifies what is meant by the phrase: "As used herein, this phrase means that the mononuclear cells can be treated, for example by exposure to a source of ionizing radiation, which will have the effect of preventing lethal GvHD. It is believed that the treatment *sufficiently hinders the mononuclear cell proliferation* such that they do not cause a lethal GvHD in the patient" (*id.* at col. 4, ll. 42-47 (emphasis added)).

The Examiner has rejected the claims under 35 U.S.C. § 103 as unpatentable over the combined teachings of Waller and Sykes, but the Examiner's underlying rationale appears to be one of anticipation, rather than obviousness.

For example, the Examiner concedes that "Waller do[es] not explicitly teach[ ] that [the] treated T cell[s] retain their ability to proliferate" (Answer 5), but argues that "Waller teaches that said treatment sufficiently hinders the mononuclear cell proliferation such that they do not cause a lethal GvHD" and "stress[es] that said treated T cell[s] should be viable" (*id.*), while the present Specification teaches that "[t]he mononuclear cells are incubated with a sufficient concentration of a cytotoxic drug so as to substantially reduce their ability to cause GvHD" and a "sufficient concentration is that *which causes greater than 90% inhibition of the proliferation of treated cells*" (*id.*).

In addition, the Examiner argues that "Sykes [ ] specifically stress[es] that [ ] treatment should not completely eliminate[ ] T cells . . . [t]herefore it would be obvious . . . to deduce that said non-eliminated T cells would be able to retain their ability to proliferate in the recipient" (Answer 5). So,

rather than relying on Sykes to provide a reason for combing teachings to meet the claim limitations, the Examiner appears to be relying on the reference as evidence that fludarabine treated T cells retain their ability to divide and proliferate. *See In re Samour*, 571 F.2d 559, 563, 197 USPQ 1, 4-5 (CCPA 1978).

Finally, the Examiner asserts that Waller "uses fludarabine treatment to prevent treated cells from causing GvHD[,] not to reduce T cell population" (Answer 7), and "it can be assumed [Waller's] method will obviously perform the claimed process" (*id.* at 9).

Thus, the Examiner's underlying rationale appears to be that the present Specification teaches that the mononuclear cells need only retain a minimal ability to proliferate (i.e., less than 10% of their original capacity), and Waller *really* teaches that the mononuclear cells can retain the ability to proliferate a little, as well. In other words, the Examiner's rationale appears to be that both Waller and the present Specification teach the same thing, and that Waller anticipates the claimed invention.

A prior art reference may anticipate even when claim limitations are not expressly found in that reference, but are nonetheless inherent in it. *See, e.g., Atlas Powder Co. v. IRECO Inc.*, 190 F.3d 1342, 51 USPQ2d 1943 (Fed. Cir. 1999); *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985). Moreover, "when considering a prior art method, the anticipation doctrine examines the natural and inherent results in that method without regard to the full recognition of those benefits or characteristics within the art field at the time of the prior art disclosure."

Perricone v. Medicis Pharm. Corp., 432 F.3d 1368, 1378, 77 USPQ2d 1321, 1327 (Fed. Cir. 2005).

"[T]he Patent Office has the initial burden of coming forward with some sort of evidence tending to disprove novelty." *See In re Wilder*, 429 F.2d 447, 450, 166 USPQ 545, 548 (CCPA 1970). Nevertheless, "when the PTO shows sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 708, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Similarly, "where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may, in fact, be an inherent characteristic of the prior art, it possesses the authority to require the applicant to prove that the subject matter shown to be in the prior art does not possess the characteristic relied on." *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). Shifting the burden under these circumstances is reasonable because of "the PTO's inability to manufacture products or to obtain and compare prior art products." *Id.* at 1255, 195 USPQ at 433-34.

The issue raised by this appeal, then, is whether the prior art provides a reasonable basis for shifting the burden to Appellants to establish that Waller's mononuclear cells do not retain *some* ability to proliferate, even if drastically diminished. However, we find that this issue has not been developed on the record in a manner susceptible to meaningful review.

On the one hand, we note the Examiner's assertion that "both Waller [ ] and the instant Specification use[ ] similar concentrations of cytotoxic chemotherapeutic drugs to treat mononuclear cells and administer[ ] similar

amount[s] of treated mononuclear cells to facilitate engraftment of transplanting hematopoietic cells . . . Thus, it is clear that both the prior art and the instant claims administer[ ] the same treatment to the same patients to achieve the same results" (Answer 8-9). However, the Examiner has not pointed to or analyzed any *particular* facts in evidence in support of this assertion.

On the other hand, we note Appellants' argument that "Waller specifically discloses that the mononuclear cells should not proliferate" and that "[t]his is exactly the opposite of the claimed method" (Appeal Br. 6). But this argument does not satisfactorily dispose of the matter because it does not address Waller's qualification of what is meant by the phrase "'. . . incapable of proliferating and causing a lethal GvHD effect'" (Waller, col. 4, ll. 40-41). As discussed above, Waller qualifies the phrase as follows: "As used herein, this phrase means that the mononuclear cells can be treated, for example by exposure to a source of ionizing radiation, which will have the effect of preventing lethal GvHD. It is believed that the treatment *sufficiently hinders the mononuclear cell proliferation* such that they do not cause a lethal GvHD in the patient" (*id.* at col. 4, ll. 42-47 (emphasis added)). In our opinion, a reasonable inference is that Waller's mononuclear cells retain a minimal ability to proliferate, but not enough to trigger a lethal GvHD effect.

In summary, there is at least some evidence of record supporting the Examiner's assertion that that the claimed invention is anticipated by Waller, but that evidence has not been addressed or presented in a manner that gives Appellants a full and fair opportunity to respond. Accordingly we remand the application to the Examiner to take appropriate action based on the issues discussed above. Any further communication from the Examiner which contains a rejection of the claims should provide Appellants with a full and fair opportunity to respond.

REMANDED

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